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HAVE WE ANY THERAPEUTIC MEANS

AS PROVEN BY EXPERIMENT,

WHICH DIRECTLY AFFECT THE LOCAL PROCESSES OF INFLAMMATION?

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HAVE WE ANY THERAPEUTIC MEANS, AS PROVEN BY EXPERIMENT, WHICH DIRECTLY AFFECT THE LOCAL PROCESSES OF INFLAMMATION?

BELIEVING that the true aim of a paper read before this Association should be merely the indication of the salient points of the subject, in order to elicit as full discussion as possible, I shall omit all such details as are non-essential. It will be impossible for me, in the time assigned, to answer the query forming the title of my paper except with regard to the early stages of inflammation. Owing to press of work, I have also been unable to pursue my investigations as far as I had wished, and should therefore prefer to entitle my paper "A preliminary note as to whether we possess any therapeutic means, as proven by experiment, which directly influence the local processes of inflammation." I trust that any apparent neglect to specifically mention the sources of my knowledge will be set down to the necessary brevity of this paper, and to the fact that all of you must be more or less familiar with the sources whence my facts are culled.

Careful study of the essential processes of various morbid conditions, has often led to the theoretical

employment of therapeutic measures, which by their apparent practical use have confidently encouraged their future employment. Clinical proofs, however, always embody the inherent weaknesses of careless or prejudiced observation, with the varying unknown quantity of the effects of the *vis medicatrix naturæ*.

But if in addition we find by experiment that our *a priori* therapeutics when experimentally applied in the case of animals, actually produce the precise effects which we have pre-determined will probably prove efficacious, then we can hardly go astray in confidently applying similar treatment to the human subject. If now we find clinical descrepancies, it must be our aim to ascertain the exact limitation of the remedy for good or evil, and the precise indications for its employment, instead of thrusting it contemptuously aside, when we fail of the expected result, the failure being probably our faulty method of applying the treatment and not self-inherent. Upon the other hand we must always hold before our eyes the experimental mirror of what has been and can be effected, and not expect to do what we have demonstrated is an impossibility.

This paper is avowedly written in advocacy of bloodletting in general, but chiefly of the local abstraction of blood. This once much-vexed question seems again pressing for solution, as the pendulum of unreasoning prejudice and authority, having reached its furthest limit on the side of proscription, is now slowly swinging back to an opposite point, the stability of which must depend upon

the possibility of satisfactorily answering the question contained in my title. If the answer be favorable, the revival of bloodletting will be founded upon the only sure basis, viz., that of demonstrated scientific facts which will replace the purely theoretical dicta of authority, which, like the will-o'-the-wisp, led our forefathers into such an erratic use of the lancet that it wrought not only by its abuse its cure, but an almost total abolition of bloodletting, which I for one regret.

A rapid review of the minute processes of the earlier stages of inflammation, coupled with a consideration of some facts relating to the physiology of nutrition, will form a necessary preface to the body of my paper. I shall refer only to the early stages of inflammation, for, of course, no direct effect can be exerted upon the tissue changes of that process, when the inflamed part has returned to its fœtal state—is merely embryonal tissue, only a step further from which is pus.

Examining with a low power, we find that the arteries are normally about one-sixth smaller than the veins, and that "in every artery a space can be distinguished within the outline of the vessel, which is entirely free from corpuscles." The arterial current is the more rapid, and it is appreciably accelerated at each beat of the heart. As to whether there is or is not a primary contraction of the arteries in the first stages of inflammation seems to depend so much upon the irritant used that I shall pass the question by as unimportant for our present purposes. The first change noted is an enlarge-

ment of the arteries, which become tortuous, the veins following suit; but there is "a time when, instead of the arteries being sensibly smaller" than the veins, "they far exceed them in diameter." Note this fact carefully. Contrary to expectation, at the outset the circulation is accelerated in the dilated vessels, but the rate soon becomes normal, and is succeeded by a slowing, then an oscillatory movement, a temporary stagnation; again a resumption of the flow, and finally permanent stasis, with crowding of the vessels—the veins especially—with cell-elements, so that the previous clear space existing along the walls of the arteries can no longer be detected.

The obstructions seem to consist solely of red cells, which are so closely packed as to render "their individual forms" . . . "scarcely distinguishable." Free diapedesis of the white-blood corpuscles now takes place, with exudation of liquor sanguinis, both processes having commenced when incipient stagnation set in. The experiments of Ryneck and H. Weber have demonstrated "that in an injured part, the walls of the capillaries become so altered that the liquor sanguinis, instead of transuding from the smaller arteries in quantities just sufficient to balance the absorption, leaks abundantly from the vessels, and that in many cases this is subsequently associated with squeezing out of the leucocytes, or even of the colored corpuscles." The consequence of this free exudation is that, owing to increased pabulum—liquor sanguinis—the cells of the inflamed area multiply until,

in many instances, we have the tissue reverting to the fœtal state, when it consists merely of embryonal tissue—viz., a mass of indifferent cells held together by a small quantity of intercellular cement, which latter has only to liquefy, and *pus* at once results.

The remaining subsidiary phenomena of inflammation being non-essential, are purposely omitted.

To summarize the whole process in the words of Dr. Burdon-Sanderson, "the circulation is at first accelerated and increased, subsequently retarded and diminished," and "the latter condition is attended with exudation of liquor sanguinis, migration of leucocytes, and stasis."

That the primary acceleration of the blood-stream is in some way dependent on reflex nerve action seems clear. At this point, our researches into the essential phenomena of inflammation may cease. A few physiological facts demand consideration before I sum up what *a priori* reasoning indicates as to the therapeutics of the early stages of inflammation. Ranvier has shown that the white-blood cell is sluggish, and then ceases to move in the absence of oxygen, and is active in proportion to the amount of that substance present. It is also indisputable that the red cells are the main carriers of oxygen, and that if their numbers are relatively increased to the fluid in a given bulk of blood, especially if, as in inflammation, both the necessity and capability of the cells of the tissue making use of the oxygen are removed, at once an excess of oxygen obtains, *i. e.*, an increased amœboid action of the white cells not only is possible, but becomes a necessity.

Physiology teaches us that only so much of the constituents of the blood-plasma exude or are withdrawn by cell action as suffice for the normal function of the parts, and that, if any excess is present, that the lymph-spaces return it into the lymphatics, whence it passes into the general circulation. If, however, the lymph-spaces are compressed by dilated bloodvessels, and crowded with migrated cell-elements, the excess of pabulum must be retained, with a consequent stimulus to undue cell-proliferation. Precisely this obtains in inflammation. But physiology likewise shows us that there is a certain attraction exerted upon the blood-current by the tissue-cells according to their varying wants which not only aids the *vis-a-tergo* action of the heart, but actually determines to a certain extent the amount of blood present at any given time, for instance, in a gland. If this action obtains in health, there is no reason to doubt it is still more potent in disease. From the physiological fact upon the one side that only so much pabulum is withdrawn as suffices for healthy function, and, on the other, that in inflammation this material is in great excess, it seems proven, viewed from the light thrown upon the subject by the experiments of Ryneck and Weber, that, in some way, the capillary walls are injured by intra-vascular pressure.

To summarize: (1) Intra-vascular pressure injures the vessel-walls, aided, perhaps, by the constant passage of the white cells; in consequence, an inordinate amount of blood-plasma exudes, which stimulates cell-proliferation. (2) The accumulation

and stagnation of the red-blood cells, with the draining-off of the liquor sanguinis, cause a relative excess of oxygen, which excites to increased amœboid action the white-blood cells and their consequent migration. By the study of the phenomena of osmosis, we learn that stagnation of fluid and intra-vascular tension induce outflow; but reverse the latter condition, increase the rapidity of the circulation, and, with the constitution of the blood, an outflow must result.

From these studies I am forced to conclude that a theoretically perfect remedy for incipient inflammation must comprehend the following effects. It must either lessen the *vis-a-tergo* of the heart's action—so as to prevent injury to the vascular walls by over-distention and the consequent outpouring of liquor sanguinis; it must prevent such an ingress of blood into the affected area as would produce the excess of oxygen, the migration of cells, the blocking up of the lymph-spaces, etc.; or what would practically amount to the same thing, it must so lessen the difficulty of escape on the venous side, that howsoever great the *vis-a-tergo*, a ready draining off, nay, aspiration, as it were, of the venous blood may occur; if possible, both these effects must be produced. The last requisite would be that the remedy must increase the frequency while it lessens the force with which the heart acts, for although, whatever, would lessen the *vis-a-tergo* would prevent any further outpouring of pabulum, yet that which was already exuded must remain, and would have to be consumed before the initiated cell-change

could cease. In my experiments on the frog's tongue I noted all the vascular changes described in the earlier part of this paper. When the stasis was complete, a large vein on the distal side was divided, *i. e.*, local bleeding was effected from the vessels directly leading from the inflamed area. I purposely avoided opening the vein on the cardiac side of the phlogosed spot lest I might simultaneously divide the supplying artery. By severing one of the ranine veins at a point where I could distinctly see that the venous radicles of the inflamed area emptied, I achieved my purpose without further damage.

The effect upon the obstructed vessels was first an oscillation of the blood disks, then an occasional momentary flow of blood, then suddenly a rapid resumption of the circulation sweeping out the bloodvessels, and apparently restoring them to their normal condition, except at spots where the agents inducing the inflammation had chemically destroyed the vessels or coagulated their contents. I do not presume to say that the white corpuscles betook themselves at once back again into the bloodvessels, for I did not use sufficient amplifying power to observe this, nor was I then dealing with any other processes than the vascular changes. I should have carried my researches much further had I not seen that nothing was needed beyond a mere corroboration of Gensmer's admirable paper, which I shall now quote:

"At the present time it is generally accepted, that by local bleeding inflammatory stasis is re-

lieved, but this view has not been demonstrated; many adhere to the derivative action of bleeding and many still believe in the loss of blood as such, in the amount of blood drawn. The web of the foot of a curarized frog, was burnt with a red-hot pointed needle, or with nitrate of silver." . . . "As soon as" . . . "slowing of the current and stasis had taken place, a leech was placed near the hock-joint." . . . "As soon as sucking began, the picture under the microscope changed in a striking manner. The blood-current was immediately accelerated, blood corpuscles which adhered to the wall passed into the blood-current, stasis was relieved, briefly, the inflamed capillary loops were in a short time, sometimes in a few minutes, entirely free, and presented in a few cases at the termination of the experiment, the appearance of a perfectly normal and even accelerated circulation." The authors were unable positively to determine whether the migrated white-blood cells "were in any way influenced by the bleeding." Owing to the tardy rate with which the blood was effused after scarification, the author stated that the good effects were not comparable to those of leeching. In like manner general bloodletting by opening an abdominal vein was inferior to leeching near the affected area. Dr. Gensmer considers it proven "that the antiphlogistic effect of local bleeding is due to a purely mechanical cause. Through the stronger current caused by the sucking of the leech (or by a cupping-glass, or by scarification) is the blood corpuscle which adheres to the

wall in the inflamed territory torn away, the obstructed capillary perfectly opened and there is a normal, indeed a temporarily stronger circulation established." . . . "Local bleeding prevents stasis. Bleeding not only does not cause local anæmia, but even occasions (of course transiently) arterial hyperæmia, that is, it causes a more intense flow of arterial blood to the inflamed point. Further, this abundant supply of arterial blood results in a better nourishing of the tissue, and that, therefore, the tissue is better able to withstand the effects of the inflammatory process is to be expected. It further follows that the antiphlogistic effect of bleeding depends upon the quantity of blood drawn, and that in the first place only the rapidity of the current is to be considered. Evidently the bleeding must take place when possible between the inflamed point and the heart, and not far from the former."[1]

What the effects of bloodletting are upon the general circulation has an important bearing upon the subject we are now discussing. According to the latest authority, "The water is increased, and the globules," . . . oxygen carriers, "*are diminished* in relative amount." . . . "The action of the heart becomes *more rapid* and its force lessens"—the italics are mine—"the arterial tension falls." But how about the evil effects of bloodletting? "It is a remarkable fact perfectly well

[1] Dr. Alfred Gensmer Halle. Centralblatt für die medizinschen Wissenschaften, April 1, 1882.

known to old practitioners, and to which Sir James Paget has recently called attention, that the ill-effects of bleeding in healthy subjects are very temporary and easily repaired. The blood globules, which are relatively more affected by bleeding than the other constituents, are quickly reproduced." . . . As surgeons, we must all have had ample proof of this fact. Some years since while pursuing other investigations upon human blood, I observed the same fact and noted it in the published report of my work. I need hardly point out, that if my experiments with those of Gensmer's are reliable, and the other facts quoted are really facts, our ideal remedy is found. From the quotations given of Gensmer's paper, it is clear that our experimental results exactly tally. I think, however, that the superior advantages of leeching over scarification, etc., can hardly be similarly obtained in the human subject since the relative size of the leech to the frog must have had a considerable share in effecting the good obtained by an actual aspiration of the blood. In my own experiments, by dividing a large vein in the tongue, I obtained the effect of bloodletting pure and simple. To produce the best results, then, we should, when possible bleed from one of the principal veins leading from the inflamed focus. When this is impossible, leeching or wet-cups should be resorted to, since by both the mechanical effects of aspiration are superadded to the mere outflow of blood. But many authorities maintain that bloodletting can be dispensed with in all cases, for exactly the same results are obtained

by the use of arterial sedatives. To test the truth of such statements it is only requisite to experimentally induce inflammation, and then give a large dose of gelsemium. The arteries are seen to become smaller, the current slower, and if stagnation has already occurred, it increases or remains stationary. This and similar remedies then reverse that which both upon theoretical and experimental grounds we have found to be most effectual. They certainly also interfere with the rapid absorption of effusions.

From a review of the facts set forth in this paper, I think I am warranted in stating the following propositions as the logical and practical outcome of my investigations:

(1) During the stage of dilated arteries, with increased rapidity of the current, but little danger of capillary changes with exudation need be apprehended, and here perhaps ergot, certainly arterial sedatives do good, either directly or indirectly, without bloodletting, by reducing the size and rapidity of the current, thus allowing the veins of the irritated area time to empty themselves, even of an unaccustomed amount of blood. Thus if vascular-pressure changes have taken place, the vessels have an opportunity to return to the norm.

(2) After stasis has occurred, or while it is occurring, weakening of the heart's action and a diminished volume of the current—*e. g.*, the effect of arterial sedatives—can do nothing but harm to the inflamed area, although, for the reasons given in proposition 1, it may prevent extension of in-

flammation in the circumjacent parts, which are merely in the earlier stages of congestion.

(3) The results to be sought, and which are secured by local bloodletting, are removal of the blood on the venous side, so that the vessels can not only empty themselves, but a certain amount of *vis-a-fronte*—*i. e.*, aspiration—is invoked: this secondarily results not only in a temporary return to the norm on the arterial side, but an increased rapidity (and here is an important point)—lessened force of the circulation. The acceleration of rate without the weakened force of the circulation would further damage the vessels, instead of which the increased rate of the current merely serves to sweep out the accumulated red-blood cells, the cause of the excess of oxygen, and the consequent cell-migration. The vehement current also induces a rapid resorption of the effused liquor sanguinis, at once the stimulator to growth, and the food of the cells. This latter advantage is not founded on theory alone, for it is a matter of common observation that the mere amount of blood extracted produces no sensible effects on an inflamed breast, for instance, *at first*, but in a few hours, the skin, if carefully examined, has become wrinkled, and the organ shrunken. This effect is secondary to the loss of blood, and chiefly results from the absorption of the inflammatory exudate.

(4) Arterial sedatives in the later stages are usually inadmissible except as succedanea to bloodletting, as far as the focus of inflammation is concerned: the surrounding parts, which are merely

congested, may be benefited by their exhibition. After bloodletting, they act favorably, because, when the stasis has been overcome, they lessen intra-vascular pressure, and thus permit the blood-vessels to recover their normal condition. They also alleviate pain by lessening the bulk of blood in the part—*i. e.*, they relieve nerve-pressure.

As before intimated, this essay is in reality little more than a few notes on the effects of local blood-letting, and does not pretend to cover the extended field of either the local or general treatment of inflammation. If my remarks prove fruitful in the way of an instructive discussion, which may induce some of my hearers to resort anew to this useful but neglected remedy, I shall feel amply rewarded.